**Structural MRI detects progressive regional brain atrophy and neuroprotective effect of SSRI in N171-82Q Huntington’s disease mouse model**

Yong Cheng 1#, Qi Peng1#, Zhipeng Hou2#, Manisha Aggarwal2, Jiangyang Zhang2 , Susumu Mori2,3, Christopher A. Ross1,4,5, and Wenzhen Duan1 \*

1Division of Neurobiology, Department of Psychiatry and Behavioral Sciences; 2Department of Radiology; 3F.M. Kirby Functional Imaging Center, Kennedy Krieger Institute, Baltimore, MD 21205; 4Department of Neuroscience; 5Department of Neurology,Johns Hopkins University School of Medicine, Baltimore, MD 21287.

\*Correspondence: Wenzhen Duan, Division of Neurobiology, Department of Psychiatry, Johns Hopkins University School of Medicine, CMSC 8-121, 600 N. Wolfe Street, Baltimore, MD 21287.

Phone 410 502-2866. FAX 410 614-0013. Email: [wduan2@jhmi.edu](mailto:wduan2@jhmi.edu)

# These authors contributed equally to this work

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**Abstract**

Huntington’s disease (HD) displays progressive striatal atrophy that proceeds long before the onset of clinical motor symptoms and ultimately widespread brain atrophy and impairment of brain function. Neuroprotective agents should have potential to prevent cell loss before clinical symptoms arise. Biomarkers that could predict disease onset as well as evaluate neuroprotection are needed. Studies suggest structural MRI measures could be considered as such biomarkers for presymptomatic as well as symptomatic clinical trials of HD. However, whether MRI measures are sensitive to detect treatment response is not known. HD mouse models exhibit both behavioral and neuropathological features resembled to HD, and are widely used in preclinical therapeutic trials. There has been relatively little study of *in vivo* longitudinal brain atrophy in relation to other phenotypes and most importantly, in response to neuroprotective treatments in HD mouse models. We used micro MRI technology T2-weighted images combined with automated morphological analysesand characterized regional brain volume changes longitudinally in N171-82Q mice, one of widely used fragment HD mouse models in preclinical studies. We report here that MRI detects adult-onset and progressive brain atrophy in the striatum, neocortex and several other brain regions in N171-82Q mice; the progressive atrophy in striatum and neocortex is positively correlated with motor deficits; most notably, MRI is sensitive to detect neuroprotective effects of SSRI longitudinally in HD mice. This is the first longitudinally MRI study to provide evidence that structural MRI measures can detect the therapeutic effect in HD mouse model, suggesting that structural MRI measures in brain could be considered as valuble biomarkers in HD clinical trials.